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| - | INFORMATION DI | SCLO | SURE | Application Number | 10/664,421-10/789,818 N-AL | | |
| | STATEMENT BY | | | Filing Date | 09/16/2003 | | |
| | | | • | First Named Inventor | Ryan Bremer | | |
| | | | | Group Art Unit | 1656 | | |
| | (use as many sheets | as ne | cessary) | Examiner Name | Nashed | | |
| Sheet | 1 | of | 4 | Attorney Docket Number | 039363-0703 | | |

| | U.S. PATENT DOCUMENTS | | | | | | | | |
|--------------------|-----------------------|---------------|---|---|------------------------------|--|--|--|--|
| Examiner Initials* | Cite No. | U.S. Patent D | ocument | Name of Patentee or Applicant of Cited Document | Date of Publication of | Pages, Columns, Lines, Where Relevant | | | |
| | | Number | Kind Code ² (if known) | | Cited Document MM-DD-YYYY | Passages or Relevant Figures Appear | | | |
| NN | A1 | 20010008765 | | Shinoki et al. | 07/19/2001 | | | | |
| | A2 | 20010012537 | | Anderson et al. | 08/09/2001 | | | | |
| | A3 | 20010014448 | | Chappa et al. | 08/16/2001 | | | | |
| | A4 | 20010014449 | | Nerenberg et al. | 08/16/2001 | | | | |
| | A5 | 20010016322 | | Caren et al. | 08/23/2001 | | | | |
| | A6 | 20010018642 | | Balaban et al. | 08/30/2001 | | | | |
| | . A7 | 20010019827 | | Dawson et al. | 09/06/2001 | | | | |
| /\/ | A8 | 6100254 | | Budde et al. | 08/08/2000 | • | | | |
| NN | A9 | 6197495 | | Qui et al. | 03/06/2001 | | | | |

| ŕ | | | UNPUBLISH | HED U.S. PATENT APPLICATION | DOCUMENTS | |
|--------------------|--------------------------|----------------|---|---|------------------------------|--|
| Eversions | Cito | U.S. Patent Ap | • | Name of Patentee or Applicant of Cited Document | Filing Date of | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
| Examiner Initials* | Cite No. ¹ | Serial Number | Kind Code ² (If known) | | Cited Document MM-DD-YYYY | |
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|-----------------------|--------------------------|--------------|--|--|---|--|--|----------------|
| Examiner Initials* | Cite No. ¹ | Fo Office | oreign Patent [3 Number ⁴ | Occument Kind Code ⁵ (If known) | Name of Patentee or Applicant of Cited Documents | Date of Publication of Cited Document MM-DD-YYYY | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear | T ⁶ |
| NN | A10 | wo | 99/26966 | | The Regents of the University of California | 06-03-1999 | | |
| NN | A11 | wo | 01/58951 | | Stichting Voor de Technische Wetenschappen | 08-16-2001 | | |
| NN | A12 | wo | 02/24722 | | Prochon Biotech Ltd. | 03-28-2002 | | |

| NON PATENT LITERATURE DOCUMENTS | | | | | | | |
|---------------------------------|--------------------------|--|----------------|--|--|--|--|
| Examiner Initials* | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published. | T ⁶ | | | | |

| Examiner Signature | /Nashaat Nashed/ (01/30/2007) | Date Considered |
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^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

MODIFIED PTO/SB/08 (08-00)

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U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

perwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control

| | Substitute for for | m 1449B/ | PTO | · Complete if Known | | | |
|-------|--------------------|-----------|----------|------------------------|-----------------------------|--|--|
| | INFORMATION | DISCLO | SURE | Application Number | -10/664,421- 10/789,818 Not | | |
| | STATEMENT BY | Y APPLI | CANT | Filing Date | 09/16/2003 | | |
| | • | | | First Named Inventor | Ryan Bremer | | |
| 1 | | | | Group Art Unit | 1656 | | |
| | (use as many shee | ets as ne | cessary) | Examiner Name | Nashed | | |
| Sheet | 2 | of | 4 | Attorney Docket Number | 039363-0703 | | |

| | | NON PATENT LITERATURE DOCUMENTS | |
|--------------------|--------------------------|--|----------------|
| Examiner Initials* | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published. | T ⁶ |
| NN A13 | | BOEHM, et al., "Novel Inhibitors of DNA Gyrase: 3D Structure Based Biased Needle Screening, Hit Validation by Biophysical Methods, and 3D Guided Optimization. A Promising Alternative to Random Screening," J. Med. Chem. 43:2664-2674 (2000) | , |
| | A14 | BOHACEK, et al., "Multiple Highly Diverse Structures Complementary to Enzyme Binding Sites: Results of Extensive Application of a de Novo Design Method Incorporating Combinatorial Growth," J. Am. Chem. Soc. 116:5560-5571 (1994) | |
| | A15 | CHONG, et al., "Molecular dynamics and free-energy calculations applied to affinity maturation in antibody 48G7," PNAS 96:14330-14335 (1999) | |
| | A16 | CORNELL, et al., "A Second Generation Force Field for the Simulation of Proteins, Nucleic Acids, and Organic Molecules," J. Am. Chem. Soc. 117:5179-5197 (1995) | |
| | A17 | DONINI and KOLLMAN, "Calculation and Prediction of Binding Free Energies for the Matrix Metalloproteinases," J. Med. Chem. 43:4180-4188 (2000) | |
| | A18 | DOWNS and WILLETT, "Similarity Searching and Clustering of Chemical-Structure Databases Using Molecular Property Data," J. Chem. Inf. Comput. Sci. 34:1094-1102 (1994) | |
| | A19 | ELCOCK, Realistic modeling of the denatured states of proteins allows accurate calculations of the pH dependence of protein stability. J. Mol. Biol., 294:1051-1062, (1999). | |
| | A20 | FELDER, "The Challenge of Preparing and Testing Combinatorial Compound Libraries in the Fast Lane, at the Front End of Drug Development," Chimia 48:531-541 (1994) | |
| | A21 | GILLILAND and LADNER, Crystallization of biological macromolecules for X-ray diffraction studies. Current Opinion in Structural Biology, 6:595-603, 1996. | |
| | A22 | JARVIS and PATRICK, "Clustering Using a Similarity Measure Based on Shared Near Neighbors," IEEE Transactions on Computers 11:1025-1034 (1973) | |
| | A23 | KE and DOUDNA, Crystallization of RNA and RNA-protein complexes. Methods, 34:408-414, (2004). | |
| NN | A24 | MASSOVA and KOLLMAN, "Computational Alanine Scanning to Probe Protein – Protein Interactions: A Novel Approach to Evaluate Binding Free Energies," <i>Journ. of Amer. Chem. Soc.</i> 121(36):8133-8143 (1999) | |

| Examiner /Nashaat Nashed/ (01/30/2007) | Date Considered | |
|--|--------------------|--|
|--|--------------------|--|

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that Issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

Approved for use through 10/31/2002. OMB 0651-0031 U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control

| | Substitute fo | or form 1449B | /PTO | Complete if Known | | | |
|-------|---------------|---------------|----------|------------------------|----------------------------|--|--|
| | INFORMATI | ON DISCLO | SURE | Application Number | 40/664,424 10/789,818 NFST | | |
| | STATEMEN | T BY APPLI | CANT | Filing Date | 09/16/2003 | | |
| | | | • | First Named Inventor | Ryan Bremer | | |
| | | | | Group Art Unit | 1656 | | |
| | (use as many | sheets as ne | cessary) | Examiner Name | Nashed | | |
| Sheet | 3 | of | 4 | Attorney Docket Number | 039363-0703 | | |

| NON PATENT LITERATURE DOCUMENTS | | | | | | | | |
|---------------------------------|--------------|--|----------------|--|--|--|--|--|
| Examiner Initials* | Cite No.1 | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published. | T ⁶ | | | | | |
| NN | A25 | MCGOVERN, et al., "A Common Mechanism Underlying Promiscuous Inhibitors from Virtual and High-Throughput Screening," J. Med. Chem. 45:1712-1722 (2002) | | | | | | |
| | A26 | OBRECHT, et al., "Solid-Supported Combinatorial and Parallel Synthesis of Small Molecular Weight Compound Libraries," <i>Linker Mel. & Cleav. Stret.</i> P. 85. Incomplete citation. | - | | | | | |
| NN | A27 | OWEN, et al., "Two Structures of the catalytic domain of phosphorylase kinase: an active protein kinase complexed with substrate analogue and product," Curr. Biol. Ltd. 3:467-482 (1995) | | | | | | |
| NN | A28 | PEARLMAN and CHARIFSON, "Are Free Energy Calculations Useful in Practice? A Comparison with Rapid Scoring Functions for the p38 MAP Kinase Protein System," <i>J. Med. Chem.</i> 44:3417-3423 (2001) | | | | | | |
| NN | A29 | RIPKA, et al., "Aspartic Protease Inhibitors Designed from Computer-Generated Templates Bind as Predicted," Org. Lett. 15:2309-2312 (2001) | | | | | | |
| NN | A30 | WIENCEK, New strategies for protein crystallization growth. Ann.Rev.Biomed.Eng., 1:505-534, (1999). | | | | | | |
| NN | A31 | WILLETT, "Chemical Similarity Searching," J. Chem. Inf. Comput. Sci. 38:983-996 (1998) | | | | | | |

| | | T | · |
|-----------------------|-------------------------------|--------------------|---|
| Examiner Signature | /Nashaat Nashed/ (01/30/2007) | Date Considered | |

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

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| | Substitute for form 1449B/PTO | | | Complete if Known | | |
|-----------------------------------|-------------------------------|---------------|-------------|------------------------|-----------------------|--|
| INFORMATION DISCLOSURE | | | SURE | Application Number | 19/664,421 10/789,818 | |
| ٠. | STATEMENT BY APPLICANT | | Filing Date | 09/16/2003 | | |
| | • | | | First Named Inventor | Ryan Bremer | |
| | | | | Group Art Unit | 1656 | |
| (use as many sheets as necessary) | | Examiner Name | Nashed | | | |
| Sheet | 4 | of | 4 | Attorney Docket Number | 039363-0703 | |

| | | NON PATENT LITERATURE DOCUMENTS | |
|-----------------------|--------------|--|----------------|
| Examiner Initials* | Cite No.1 | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published. | Т ⁶ |
| NN | A32 | YANG et al., Peptide analogs from E-cadherin with different calcium-binding affinities. J. Peptide Research, 55:203-215, 2000. | |

| Examiner Signature | /Nashaat Nashed/ (01/30/2007) | Date Considered | ٠. |
|-----------------------|-------------------------------|--------------------|----|
| | | | |

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of Information unless it contains a valid OMB control

| Substitute for form 1449/PTO | Complete if Known | | |
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| / In Interpretation disclosure | Application Number | 10/789,818 | |
| DEC 1 8 200 STATEMENT BY APPLICANT | Filing Date | 02/27/2004 | |
| \\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\ | First Named Inventor | Prabha Ibrahim | |
| | Art Unit | 1656 | |
| as many sheets as necessary) | Examiner Name | Nashed, Nashaat T. | |
| Sheet 1 of 2 | Attorney Docket Number | 039363-1202 | |

| | U.S. PATENT DOCUMENTS | | | | |
|----------------|--|-----------------|------------------|----------------------------------|--|
| Examiner Cite | | Document Number | Publication Date | Name of Patentee or Applicant of | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
| Initials* No.1 | Number-Kind Code ² (if known) | MM-DD-YYYY | Cited Document | | |
| | Al | US-5837524 | 11.17.1998 | Ochlessinger et al | |
| NN | A2 | US-5942428 | 08.24.1999 | Mohammadi et al. | |
| | A3 | U3-0100254 | 00.00.2000 | Budde et el. | |
| | A4 | US-0197495 | 03.00.2001 | Qlu et al. | |
| | | | | | |

| - | | UNPUBLISH | IED U.S. PATENT AP | PLICATION DOCUMENTS | |
|-----------------------|--------------------------|--|--|---|--|
| Examiner Initials* | Cite No. ¹ | U.S. Patent Application Document Serial Number-Kind Code ² (If known) | Filing Date of Cited Document MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
| | | | | · | |

| | | | FOREIGN PATENT | OCUMENTS | | |
|-----------------------|--------------|--|--------------------------------|---|---|----------------|
| Examiner Initials* | Cite No.1 | Foreign Patent Document Country Code ³ Number ⁴ Kind Code ⁵ (<i>if known</i>) | Publication Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Documents | Pages, Columns, Unes, Where Relevant Passages or Relevant Figures Appear | T ⁶ |
| | | | | | | |

| | | NON PATENT LITERATURE DOCUMENTS | |
|--------------------|--------------------------|--|----|
| Examiner Initials* | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published. | Т6 |
| ИЙ | A5 | Cohen et al., Molecular modeling software and methods for medicinal chemistry. Journal of Medicinal Chemistry, 33(3): 883-894, 1990. | |
| | A6 | Gilliland and Ladner, Crystallization of biological macromolecules for X-ray diffraction studies. Current Opinion in Structural Biology, 6:595-603, 1996. | |
| , | A7 | Ke and Doudna, Crystallization of RNA and RNA-protein complexes. Methods, 34:408-414, 2004. | |
| | A8 | Wiencek et al, New strategies for protein crystal growth. Annual Review of Biomedical Engineering, 91.505-534, 1999. | |

| Examiner Signature | /Nashaat Nashed/ (01/30/2007) | Date Considered | |
|-----------------------|-------------------------------|--------------------|--|

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

PTO/SB/08 (09-06)

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U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control

| | Substitute for form 1449/PTO | | | Complete if Known | | |
|-----------------------------------|------------------------------|-----------|----------|------------------------|--------------------|--|
| | INFORMATIO | ON DISCLO | SURE | Application Number | 10/789,818 | |
| STATEMENT BY APPLICANT | | | CANT | Filing Date | 02/27/2004 | |
| | | | | First Named Inventor | Prabha Ibrahim | |
| | | | • | Art Unit | 1656 | |
| (use as many sheets as necessary) | | | cessary) | Examiner Name | Nashed, Nashaat T. | |
| Sheet | 2 | of | 2 | Attorney Docket Number | 039363-1202 | |

| | NON PATENT LITERATURE DOCUMENTS | | | | | | |
|--------------------|---------------------------------|--|----------------|--|--|--|--|
| Examiner initials* | Cite No.1 | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published. | T ⁶ | | | | |
| NN | A9 | International Search Report for PCT Application PCT/US2004/005904 | | | | | |

Crossed over references are duplicates of other IDS's.

| Examiner Signature | /Nashaat Nashed/ (01/30/2007) | Date Considered |
|-----------------------|-------------------------------|--------------------|

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the Indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.18 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

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U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control

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| | Substitute for | or form 1449B/ | p(0) 4 | 83 | | Complete if Known | |
| | INFORMATI | ION DISCLO | SURE | 43/ | Application Number | 10/789,818 | |
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| • | | į | NOA P . T. | R) | First Named Inventor | Prabha Ibrahim | |
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| Sheet | 1 | of | 6 | | Attorney Docket Number | 039363-1202 | |

| | | • | | U.S. PATENT DOCUMENTS | 3 | |
|-----------------------|----------------|----------------|---|--|------------------------------|--|
| | | U.S. Patent De | ocument | | Date of Publication of | Pages, Columns, Lines, Where Relevant |
| Examiner Initials* | Cite No.¹ | Number | Kind Code ² (if known) | Name of Patentee or Applicant of Cited Document | Cited Document MM-DD-YYYY | Passages or Relevant Figures Appear |
| NN | A1 | 5698401 | | Fesik et al. | 12-16-1997 | |
| NN | A2 | 5804390 | | Fesik et al. | 09-08-1998 | |
| | /\3 | 0197495 | | Qui et al. | 03-00-2001 | |
| | A4 | 6297021 | | Nienaber et al. | 10-02-2001 | |
| NN | A5 | 6465484 | | Bilodeau et al. | 10-15-2002 | |
| | A6 | 20020048782 | | Lev et al. | 04-25-2002 | |
| | A7 | 20010008765 | | Shinoki, Hiroshi et al. | 07/19/2001 | |
| | A8 | 20010012537 | | Anderson, Norman G. et al. | 08/09 /2001 | |
| | A9 | 20010014448 | | Chappa, Ralph A ot al. | 08/16/2001 | |
| | A10 | 20010014449 | | Nere serg, Michael et al. | 08/16/2001 | |
| | A11 | 20010016322 | | Caren, Michael P. et al. | 08/23/2001 | |
| | A12 | 20010018642 | | Balaban, David et al. | 08/99/2001 | |
| | A13 | 20010019827 | | Dawson, Elliott P. et al. | 09/06/2001 | |

| | UNPUBLISHED U.S. PATENT APPLICATION DOCUMENTS | | | | | | | | | | |
|-----------|---|----------------|---|---|------------------------------|--|--|--|--|--|--|
| Examiner | Cite | U.S. Patent Ap | • | Name of Patentee or Applicant of Cited Document | Filing Date of | Pages, Columns, Lines, Where Relevant | | | | | |
| Initials* | No.1 | Serial Number | Kind Code ² (if known) | | Cited Document MM-DD-YYYY | Passages or Relevant Figures Appear | | | | | |
| | | | | | | | | | | | |

| | | | | FC | DREIGN PATENT DOCUMEN | TS | | |
|-----------------------|--------------------------|---------------------------|---------------------------------------|---|---|--|--|----|
| Examiner Initials* | Cite No. ¹ | Fo Office ³ | reign Patent D Number ⁴ | ocument Kind Code ⁵ (if known) | Name of Patentee or Applicant of Cited Documents | Date of Publication of Cited Document MM-DD-YYYY | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear | T⁰ |
| NN | A14 | EP | 0,154,734 | | Immunex Corporation | 08-29-1990 | | |
| NN | A15 | WO | 96/18738 | | Sugen, Inc. | 06-20-1996 | | |
| NN | A16 | WO | 97/46313 | | Array Technologies | 12-11-1997 | | |
| NN | A17 | wo | 98/35056 | | Merck & Co., Inc. | 08-13-1998 | | |
| NN | A18 | wo | 99/63931 | | The Salk Institute for Biological Studies | 12-16-1999 | | |
| NN | A19 | WO | 99/09217 | | Hyseq, Inc. | 02-25-1999 | | |

Crossed over references are duplicate, See other IDS's

| Examiner Signature | /Nashaat Nashed/ (01/30/2007) | Date Considered |
|-----------------------|-------------------------------|--------------------|

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| | | | | First Named Inventor | Prabha Ibrahim | | | |
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| Examiner Initials* | Cite No. ¹ | For Office ³ | reign Patent D Number ⁴ | ocument Kind Code ⁵ (# known) | Name of Patentee or Applicant of Cited Documents | Date of Publication of Cited Document MM-DD-YYYY | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear | т⁰ |
| | A20 | wo | 99/20900 | · | The Regents of the University of California | 06-03-1000 | | |
| NN | A21 | wo | 99/51773 | | Phylos, Inc. | 10-14-1999 | · | - |
| NN | A22 | wo | 01/58951 | | Stichting Voor de Technische Wetenschappen | 08-16-2001 | | |
| | A£3 | ₩ | 02/24722 | | Prechen Biotech Ltd. | 03 58 5005 | | |
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| | | NON PATENT LITERATURE DOCUMENTS | |
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| · NN | A24 | Ashani and Wilson, A covalent affinity column for the purification of acetylcholinesterase. Biochem. Biophys. Acta, 276:317-322, 1972. | |
| · · · · · · · · · · · · · · · · · · · | A25 | BOEHM, et al., "Novel Inhibitors of DNA Gyrase: 3D Structure Based Biased Needle Screening, Hit Validation by Biophysical Methods, and 3D Guided Optimization. A Promising Alternative to Random Screening," J. Med. Chem. 43:2664-2674 (2000) | |
| ! | A26 | BOHACEK, et al., "Multiple Highly Diverse Structures Complementary to Enzyme Binding Sites: Results of Extensive Application of a de Novo Design Method incorporating Combinatorial Growth," J. Am. Chem. Soc. 116:5560-5571 (1994) | |
| | A27 | CHONG, et al., "Molecular dynamics and free-energy calculations applied to affinity maturation in antibody 48G7" PMAS 96:14330-14335 (1999) | |
| NN | A28 | COE and STORER, "Solution-phase combinatorial chemistry." Molecular Diversity, 4:1-38, 1999. | |
| | AZ9 | GORNELL, et al., "A Second Generation Force Field for the Simulation of Proteins, Nucleic Acids, and Organic Molecules, J. Am. Chem. Soc. 117:5179-5197 (1995) | |
| | A30 | DONINI and KOLLMAN, "Calculation and Prediction of Binding Free Energies for the Matrix Metalloproteinases," d. Med. Chem. 43:4180-4188 (2000) | |

| Examiner | /Nashaat Nashed/ (01/30/2007) | Date | |
|-----------|-------------------------------|------------|---|
| Signature | | Considered | · |

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| | A31 | DOWNS and WILLETT, "Similarity Searching and Clustering of Chemical-Structure Databases Using Molecular Property Data," J. Chem. Inf. Comput. Sci. 34:1094-1102 (1994) | |
| | A32 | ELCOCK, Realistic modeling of the denatured states of proteins allows accurate calculations of the pH dependence of protein stability. Journal of Molecular Biology, 294:1051-1062, 1999. | |
| | A33 | FEINBERG et al., Zinc-directed inhibitors for zinc proteineses. Acta Cryst., D51: 428-449, 1995. | |
| | A34 | FELDER, F.B., The Challenge of Preparing and Testing Combinatorial Compound Libraries in the Fast Lane, at the Front End of Drug Development," <i>Chimia</i> 48:531-541 (1994) | |
| , NN | A35 | FITZGERALD et al., Crystallographic analysis of a complex between human immunodeficiency virus type 1 protease and acetyl-pepstatin at 2.0-A resolution. The Journal of Biological Chemistry, 265 (24): 14209-14219, 1990. | |
| . NN | A36 | GELLER et al., HIV-1 protease and its inhibitors in Theoretical and Computational Mthods in Genome Research. Edited by Sahai. New York: Plenum Press, 1997, p. 237-254. | |
| NN | A37 | HENDRICKSON and OGATA, "Phase Determination from Multiwavelength Anomalous Diffraction Measurements," <i>Methods of Enzymology</i> 276:494-523 (1997) | |
| NN | A38 | Diffraction (MAD): a Vehicle for Direct Determination of Three-Dimensional Structure," The EMBO Journal 9(5):1665-1672 (1990) | |
| | A89 | JARVIO and PATRICK, "Clustering Using a Cimilarity Measure Based on Chared Near Neighbors," ICEC Transactions on Computers 11:1925-1934 (1973) | |
| NN | A40 | KLEINBERG and WANKE, New approaches and technologies in drug design and discovery. Am. J. Health-Syst Pharm., 52: 1323-1336, 1995. | |
| NN | A41 | LEBL et al., "One-Bead-One-Structure," Biopolymers (Peptide Science) 37:177-198 (1995) | |
| | A42 | MASSOVA and KOLLMAN, "Computational Alanino Scanning to Probe Protein - Protein Interactions: A Novel Approach to Evaluate Binding Free Energies," Journ. of Amer. Chem. Soc. 121(36):8133-8143 (1999) | |

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| Examiner Signature | /Nashaat Nashed/ (01/30/2007) | Date Considered | |
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| | A43 | MCGOVERN, et al., "A Common Mechanism Underlying Promiscuous inhibitors from Virtual and High Throughput Screening," J. Med. Ohem. 45:1712-1722 (2002) | | | | | |
| NN | 744 | MCPHERSON et al., The Role of X-ray crystallography in structure-based rational drug designs. Chapter 6 in Chemical Structures Approaches Ration. Drug Design. Edited by D.V. Weiner et al. Boca Raton: CRC Press, 1995, p. 161-179. | | | | | |
| · NN | A45 | NAGAR et al., "Crystal Structures of the Kinase Domain of c-Abl in Complex with the Small Molecular Inhibitors PD173956 and Imatinib (STI-571)," Cancer Research 62:4236-4243 (2002) | | | | | |
| • | A46 | OBRECHT, et al., "Solid-Supported Combinatorial and Parallel Synthesis of Small-Molecular-Weight Compound Libraries," Linker Mol. & Cleav. Strat. P. 85. | | | | | |
| · | A47 | OWEN, et al., "Two Structures of the catalytic domain of phosphorylase kinase: an active protein kinase complexed with substrate analogue and product," Curr. Biol. 1d. 3:467-482 (1995) | | | | | |
| | A48 | PEARLMAN and CHARIFSON, "Are Free Energy Calculations Useful in Practice? A Comparison with Rapid Scoring Functions for the p38 MAP Kinase Protein System," <i>J. Med. Chem.</i> 44:3417-3423 (2001) | | | | | |
| | A49 | RIPKA, et al., "Aspartic Protease Inhibitors Designed from Computer-Generated Templates Bind as Predicted," Org. Lett. 15:2309-2312 (2001) | | | | | |

| Examiner | | Date | |
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| Signature | /Nashaat Nashed/ (01/30/2007) | Considered | · |

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| NN | A50 | ROSENBERRY et al., Purification of acetylcholinesterase by affinity chromatography and determination of active site stoichiometry. The Journal of Biological Chemistry, 247 (5): 1555-15565, 1972. | |
| NN | A51 | SICA et al., Affinity chromatography and the purification of estrogen receptors. The Journal of Biological Chemistry, 248 (18): 6543-6558, 1973. | |
| | | | <u>. </u> |
| | A52 | WILLETT, P., "Chemical Similarity Searching," J. Chem. Inf. Comput. Sci. 38:083-006 (1008) | |
| • | | | |
| · NN | A53 | WUTHRICH, NMR-This other method for protein and nucleic acid structure determination. Acta Cryst., D51: 249-270, 1995. | |
| | A54 | YANG FT 41 Postide analysis from F codhesis with different coloium hinding officialism lowered of Postide | |
| | | Research, 55,203-215, 2000. | |
| | | | |
| . NN | A55 | KEISS et al., Beta-Galactosidase decreases the binding affinity of the insulin-like-growth-factor-ii/mannose-6-phosphate receptor for the insulin-like-growth-factor II. European Journal of Biochemistry, 190:71-77, 1990 | |
| | A56 | BOS et al., The 500 Dalton rule for the skin penetration of chemical compounds and drugs. Experimental Dermatology, 9:165-169, 2000. | |
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| Examiner | /Nashaat Nashed/ (01/30/2007) | | Date | · |
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| NN | A57 | BOGER et al., Synthesis of a functionalized rigid bicycle[2,2,1]heptane: a useful hapten for eliciting catalytic antibodies. Journal of Organic Chemistry, 59:5078-5079, 1994. | - |
| NN | A58 | PHAN et al., Extensively methylated myosin subfragment-1; Examination of local structure, interactions with nucleotides and actin, and ligand-induced conformational changes. Biochemistry, 33:11286-11295, 1994. | |
| NN • | A59 | MARYANOFF et al., Structure activity studies on anticonvulsant sugar sulfamates related to topiramate. Enhanced potency with cyclic sulfate derivatives. Journal of Medicinal Chemistry, 41:1315-1343, 1998. | - |
| • NN | A60 | MOCHIZUKI et al., "Physical and Functional Interactions Between Pim-1 Kinase and Cdc25A Phosphatase," The Journal of Biological Chemistry 274:8659-18666, 1999 | |

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|-----------------------|-------------------------------|--------------------|--|
| Examiner Signature | /Nashaat Nashed/ (01/30/2007) | Date Considered | |

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